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# The impact of depressive symptoms on the burden of cluster headache: Results of the EUROLIGHT Cluster Headache Project, an Internet-based, cross-sectional study of people with cluster headache

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## Abstract

Many patients affected by cluster headache (CH) have a co-morbid depression. The aim of this study is to evaluate how the burden of disease is influenced by depressive symptoms measured by a depression score. The study was cross-sectional and Internet-based. We included individuals with a self-reported diagnosis of CH and asked them to fill out the EUROLIGHT questionnaire, which includes a depression score. The number of headache days was higher among patients with higher depression scores. In these participants, worrying about future attacks, avoiding triggers, believing to have earned less and avoiding to talk about the disease were more common as well. Individuals with higher depression scores reported a significantly higher burden of disease. It is possible that fear of pain, self-concealment and fear of impoverishment are consequences of the depression attributed to the headache disorder.

## Keywords

burden, cluster headache, comorbidity, depression, fear of pain, self-concealment

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## Introduction

Cluster headache (CH) is a primary headache disorder characterized by excruciating, half-sided pain accompanied by autonomic symptoms or a sense of restlessness.<sup>1</sup> The associated burden of disease is tremendous. High individual healthcare costs and high indirect costs because of absenteeism are frequent consequences of the disorder.<sup>2</sup>

Many patients suffering from chronic pain disorders have a co-morbid depression,<sup>3</sup> and CH patients are no exception in that regard.<sup>4</sup> Little is known about whether and how a co-morbid depression influences the disorder.

The aim of this study is to evaluate how the burden of disease differs between CH patients in whom psychological testing suggests a depression and those in whom it does not.

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**Table 1.** Numbers of participants and demographic characteristics per country.<sup>a</sup>

Country	Participants, <i>n</i> (%)	Sex (% male)	Age, mean (SD)	Employed or student (%)	Married or living with partner (%)
Austria	34 (3.1)	64.7	38.9 (9.2)	96.7	76.5
Belgium	31 (2.9)	67.7	42.1 (9.0)	92.3	82.8
Czech Republic	—	—	—	—	—
Denmark	11 (1.0%)	63.6	41.3 (15.7)	80.0	63.6
Finland	48 (4.4)	59.6	42.6 (12.8)	94.6	77.1
France	201 (18.6)	73.6	39.7 (10.2)	85.0	72.1
Germany	256 (23.7)	72.9	43.2 (9.5)	93.2	72.2
Ireland	5 (0.5)	60.0	47.0 (11.6)	100	100
Italy	82 (7.6)	70.7	40.1 (10.2)	92.3	87.8
Luxembourg	1 (0.1)	100	46	100.0	100
Netherlands	15 (1.4)	60.0	40.9 (13.6)	92.3	66.7
Norway	19 (1.8)	68.4	40.8 (11.0)	100.0	84.2
Poland	9 (0.8)	66.7	45.9 (7.6)	77.8	55.6
Spain	92 (8.5)	78.3	39.3 (9.0)	82.7	76.4
Sweden	43 (4.0)	65.1	43.4 (13.7)	86.5	78.0
Switzerland	41 (3.8)	80.5	40.1 (11.3)	94.4	68.3
United Kingdom	192 (17.8)	63.5	42.2 (10.8)	84.4	70.9
Total	1080	70.1	42.2 (10.8)	88.9	72.8

HADS-D: Depression subscale of the Hospital Anxiety and Depression Scale; SD: standard deviation.

<sup>a</sup>Even though some people from the Czech Republic had participated in the survey,<sup>5</sup> none of them had filled out the HADS-D.

## Methods

Design and sampling methods are described elsewhere.<sup>5,6</sup> The study was designed as cross-sectional and Internet-based; data were collected anonymously. Participants filled in the EUROLIGHT questionnaire online. Inclusion criteria were a self-reported diagnosis of CH and a residency in a European country; exclusion criteria were refusal to give informed consent and to complete the questionnaire. No incentives were offered for participation.

The depression subscale of the Hospital Anxiety and Depression Scale (HADS-D) was included in the questionnaire to determine the magnitude of depressive symptoms.<sup>5</sup> Participants indicated the extent of agreement with seven different statements on a four-point Likert-type scale allocating numerical values ranging from 0 to 3. The total score is calculated summing up the chosen values and ranges from 0 to 21. Depression is assumed in patients scoring eight or more points.<sup>7</sup>

We performed the analyses at the University Hospital Zurich using SPSS version 25 (IBM, New York, USA). Categorical variables are described as proportions and continuous variables as means and standard deviations. We used the  $\chi^2$  test to test for associations in contingency tables; their extents are reported as odds ratio (OR) with the 95% confidence interval (CI). In addition, the Mann–Whitney *U* test was used; effect sizes were calculated as published<sup>8</sup> and interpreted as large effect when  $r = 0.5$ , as medium when  $r = 0.3$ , and small when  $r = 0.1$ . Significance level was set at  $p < 0.05$ . We refer to missing data as ‘not reported’ (n.r.).<sup>6</sup>

## Results

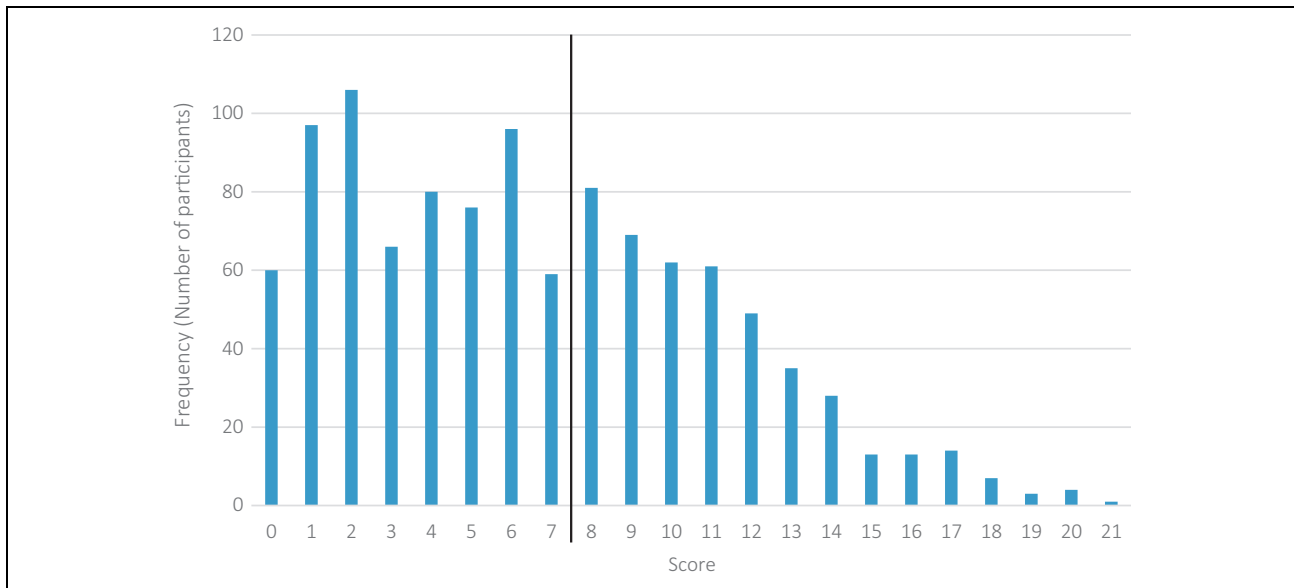
The questionnaire was completed by 1514 individuals.<sup>5</sup> We were able to confirm the diagnosis of CH in 1165 participants. Most of these participants (1080; 92.7%) answered all seven questions of the HADS-D; only their data sets were included in the further analyses. No participant from the Czech Republic fulfilled that criteria, thus, only data sets from 16 countries were included in further analyses.

Among them, 757 were male (70.1%; 2 n.r.), a majority of 88.9% (136 n.r.) was either employed or studying and 72.8% were married or living with a partner (22 n.r.). Mean age was  $42.2 \pm 10.8$  years (5 n.r.). Table 1 lists demographic data. Most of the participants (70.5%, 2 n.r.) had at least one headache day in the 30 days prior to the survey, suggesting that they were ‘in bout’.

Of those included in the analysis, 283 participants (26.7%) reported suffering from chronic CH (22 n.r.) and the validity of that diagnosis was confirmed in 234 (82.7%). When analysing the data of those suffering from chronic CH, only data sets fulfilling the criteria for chronic CH were included.

The median score reached in the HADS-D was 6.0 points. Figure 1 shows the frequency distribution. Eight or more points were reached by 440 participants (40.7%). Table 2 provides the differences between patients with higher and lower scores.

We will refer to symptoms and consequences of the disease occurring during the pain phase as ictal burden and to those occurring outside the attack as interictal burden.



**Figure 1.** Frequency distribution of the HADS score; the vertical black line indicates the cut-off above which the diagnosis of a depression is assumed. Eight or more points were reached by 40.7% of the participants. HADS: Depression subscale of the Hospital Anxiety and Depression Scale.

**Table 2.** Differences between participants with higher and lower scores in the HADS-D.

	HADS-D score <8	HADS-D score ≥8	n.r.	p Value
Number of participants	640	440	0	–
Suffering from chronic CH	15.7%	33.0%	49	<0.001
Taking preventative drugs	45.9%	56.6%	0	0.001
Having had at least one CH attack during the last 30 days	63.2%	81.3%	2	<0.001
Having hurt oneself during an attack	26.7%	50.1%	31	<0.001
Being anxious or worried about the next headache attack	61.7%	80.1%	58	<0.001
Feeling in control of the headaches ‘always’, ‘often’ or ‘sometimes’	68.1%	49.0%	10	<0.001
Feeling of family and friends understanding and accepting the headaches	85.3%	66.4%	42	<0.001
Feeling of employer and work colleagues understanding and accepting the headaches	55.8%	32.3%	244	<0.001
Avoiding to tell others about headaches	45.1%	58.3%	28	<0.001
Trying actively to avoid getting a headache	46.1%	61.8%	68	<0.001
Belief of having had a less successful career because of CH	45.3%	78.0%	25	<0.001
Belief of headaches having resulted in reduced earnings	26.8%	65.1%	92	<0.001
Having had less or no children because of CH	9.6%	24.9%	43	<0.001
CH caused a relationship break-down	7.0%	22.3%	74	<0.001

HADS-D: Depression subscale of the Hospital Anxiety and Depression Scale; n.r.: not reported; CH: cluster headache.

### Interictal burden and depression

Participants scoring eight or more points in the HADS-D reported higher numbers of (i) headache days in the last 30 days ( $p < 0.001$ ,  $r = 0.25$ , 2 n.r.), (ii) days absent from work ( $p < 0.001$ ,  $r = 0.37$ , 501 n.r.) and (iii) days unable to do any housework ( $p < 0.001$ ,  $r = 0.35$ , 487 n.r.). A higher HADS-D score was also associated with a higher number of days on which medication was taken ( $p = 0.008$ ,  $r = 0.14$ , 713 n.r.) and a higher number of attacks per 24 h ( $p < 0.001$ ,  $r = 0.19$ ).

Participants likely to suffer from a co-morbid depression reported hurting themselves during attacks more frequently

(OR = 2.760, 95% CI: 2.218–3.579;  $p < 0.001$ , 31 n.r.) and suffered from chronic CH more often (OR = 2.637, 95% CI: 1.957–3.552;  $p < 0.001$ , 49 n.r.). A prophylactic treatment was taken by them more frequently (OR = 1.534, 95% CI: 1.202–1.959;  $p = 0.001$ ).

We found no association between depressive symptoms and the number of years suffered from the disease ( $p = 0.082$ , 2 n.r.).

### Interictal burden and depression

A HADS-D score of eight or more points was associated with worrying about future attacks (OR = 2.503, 95% CI:

1.871–3.348;  $p < 0.001$ , 58 n.r.) and trying to avoid potential triggers (OR = 1.887, 95% CI: 1.462–2.435;  $p < 0.001$ , 68 n.r.). Also, participants with a higher score avoided talking to others about their disease more frequently (OR = 1.701, 95% CI: 1.326–2.182;  $p < 0.001$ , 28 n.r.).

Participants in whom psychological testing suggested a depression often believed having earned less because of their disease (OR = 5.095, 95% CI: 3.869–6.708;  $p < 0.001$ , 92 n.r.) and felt having had their career impaired by the disease (OR = 4.291, 95% CI: 3.251–5.665;  $p < 0.001$ , 25 n.r.).

Scoring eight or more points in the HADS-D was associated with more frequent reports of having had a broken relationship because of the disease (OR = 3.822, 95% CI: 2.584–5.653;  $p < 0.001$ , 74 n.r.) and having had less or no children because of the disease (OR = 3.274, 95% CI: 2.257–4.747;  $p < 0.001$ , 63 n.r.).

A feeling of being understood by colleagues and employers or by family and friends was less common among those found likely to be depressed by the test (OR = 0.369, 95% CI: 0.276–0.493;  $p < 0.001$ , 244 n.r.; OR = 0.340, 95% CI: 0.251–0.459,  $p < 0.001$ , 42 n.r., respectively). Having felt symptom-free on the last headache-free day was reported less frequently by those who scored more than eight points (OR = 0.605, 95% CI: 0.468–0.786,  $p < 0.001$ , 76 n.r.). A report of having the CH ‘rarely’ and ‘never’ as opposed to ‘always’, ‘often’ or ‘sometimes’ under control was associated with a higher score (OR = 2.223, 95% CI: 1.729–2.858;  $p < 0.001$ , 10 n.r.) as well.

## Discussion

We evaluated a large data set of CH patients from 16 European countries to study whether the presence of a co-morbid depression is associated with changes in the burden of disease. The main finding of the analyses is that both ictal and interictal burden are reported to be significantly higher by individuals with suspected depression.

Patients with higher scores in the HADS-D recounted higher numbers of headache days as well as higher numbers of days impaired by the disorder. This might be the reason for prophylactic treatment being more common in that subgroup. However, since headache frequency was assessed retrospectively, a recall bias must be expected. Interestingly, one study found that depressed children and adolescents underestimate the number of headache attacks.<sup>9</sup> If depressed adults underestimated their headache frequency, too, depression might indeed be associated with a considerably higher number of CH attacks.

In a prospective study, investigators observed that the risk of depression increases with the number of bouts per year.<sup>4</sup> It is unknown, however, whether depressions have an influence on the number of attacks, as well. A mutual influence may be suspected as depressions reduce the pain threshold in an experimental setting.<sup>10</sup> This study being cross-sectional, no conclusions about causality may be derived.

Having a higher HADS-D score was associated with not feeling symptom-free on days without pain. We did not evaluate what exactly these participants experienced, but one might speculate that depressive symptoms were referred to. For example, worrying thoughts were more common in those with higher depression scores. In addition, believing not to be in control of the disorder was stated often and might be indicative of a feeling of helplessness.

Those with higher HADS-D scores often avoided to discuss their disease with others. One wonders whether the reported lacking understanding of colleagues, employers, families and friends was a consequence of not talking to them. We do not know whether these participants had never wanted to share any details about their disease or were actively hiding them. The latter has been termed self-concealment. It is defined as ‘active concealment from others of personal information that one perceives as negative or distressing’ and is more common in people with depression.<sup>11</sup>

Avoidance of potential triggers was indicated more frequently by participants with higher scores in the depression scale. Searching for potential triggers and trying to avoid them suggests a coexisting fear of pain that is often associated with depression and may lead to increased disability.<sup>12</sup>

The feeling of having had reduced earnings and an impaired career was significantly associated with higher scores in the HADS-D. It is possible that these participants had been unable to earn money because of their headache disorder or a depression. However, we need to consider that this feeling may be a symptom of the depression as well, as the fear of impoverishment has been described as one type of depressive delusion.<sup>13</sup>

The study’s strengths are the large sample size and the large number of countries involved.<sup>5</sup> Some limitations should be noted: Even though a higher HADS-D score suggests depression and measures the extent of depressive symptoms, it cannot prove the clinical diagnosis. Despite the large number of participants, the estimated participation rate was low. In addition, it is likely that women and those severely affected by CH were over-represented.<sup>5</sup> Finally, the sample is not population-based and statistical correction of the sampling bias was not possible as information on non-participants was unavailable. Because of these latter limitations, we did not draw conclusions about incidence and prevalence. Instead, we narrowed the analysis to the investigation of relationships between subgroups and influencing factors. Given that demographic data did not suggest one subgroup having been completely missed, these conclusions are less likely to be affected by the sampling error.<sup>6</sup>

## Conclusions

Depression is a frequent co-morbidity in CH, but to date, little is known about how these disorders interact. In this article, we studied the impact of depression on the burden of disease.

Overall, both ictal and interictal burden were considerably higher in participants with suspected depression. While previous research had shown that depression may be a direct consequence of an increased ictal burden,<sup>4</sup> this study adds that the attack frequency remains high in the presence of a depression. In addition, it is likely that interictal burden, such as fear of pain, self-concealment and fear of impoverishment, might be consequences of the depression rather than the headache disorder itself.

This study highlights that pain is not the only burden that patients suffering from CH are confronted with. We wish to encourage screening every patient suffering from CH for depression. Furthermore, we propose that screening for and – if needed – treatment of mood disorders be mentioned in treatment guidelines. Prospective research is needed to understand how treating depression influences the burden of CH.

### Author contributions

Authors HP and ARG contributed equally to the study.

### Declaration of conflicting interests

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